

RECEIVED  
JUL 1 6 2003  
FEDERAL  
PATENT & TRADEMARK  
OFFICE  
1601 2800

Substitute for Form 1449 A & B/PTO				Complete if Known	
<b>O I P E</b> <b>INFORMATION DISCLOSURE</b> <b>STATEMENT BY APPLICANT</b> <b>JUL 08 2003</b> (use as many sheets as necessary)				Application Number	09/827,229
				Confirmation Number	7712
				Filing Date	April 6, 2001
				First Named Inventor	Zvia AGUR
				Art Unit	1631
				Examiner Name	Marjorie A. MORAN
				Attorney Docket Number	Q63893
Sheet 1 of 4					

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		Number	Kind Code <sup>2</sup> (if known)		
		US			

FOREIGN PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		Country Code <sup>3</sup>	Number <sup>4</sup>		

OTHER ART - NON PATENT LITERATURE DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city, and/or country where published.			
MA		R. Stoffel et al., "Thrombopoietin in Thrombocytopenic Mice: Evidence Against Regulation at the mRNA Level and for a Direct Regulatory Role of Platelets," The American Society of Hematology, Blood, vol. 87, no. 2, pp. 567-573, January 15, 1996.			
MA		Warren S. Alexander, "Thrombopoietin and the c-Mpl receptor: insights from gene targeting," The International Journal of Biochemistry & Cell Biology, pp. 1027-1035, January 28, 1999.			
MA		M. Miyazaki, et al., "The Relationship Between Carboplatin AUC and Serum Thrombopoietin Kinetics in Patients with Lung Cancer," 2 <sup>nd</sup> Department of Internal Medicine, Hiroshima University School of Medicine, Anti Cancer Research, vol. 19, pp. 667-670 (1999).			
MA		S. Vadhan-Raj, et al., "Stimulation of Megakaryocyte and Platelet Production by a Single Dose of Recombinant Human Thrombopoietin in Patients with Cancer," Annals of Internal Medicine, vol. 126, no. 9, pp. 673-681, May 1997.			
MA		H. -E. Wichmann, et al., "A Mathematical Model of Thrombopoiesis in Rats," Cell Tissue Kinet, vol. 12, pp. 551-567, January 1979.			
MA		L. A. Harker, et al., "Effects of megakaryocyte growth and development factor on platelet production, platelet life span, and platelet function in healthy human volunteers," The American Society of Hematology, Blood, vol. 95, no. 8, pp. 2514-2522, April 15, 2000.			
MA		H. Mayani, et al., "Lineage Commitment in Human Hemopoiesis Involves Asymmetric Cell Division of Multipotent Progenitors and Does not Appeal to be Influenced by Cytokines," Journal of Cellular Physiology, vol. 157, pp. 579-586, 1993.			
MA		David W. Golde, "The Stem Cell," Scientific American, pp. 36-43, December 1991.			
MA		S. J. Morrison, et al., "The Biology of Hematopoietic Stem Cells," Annu. Rev. Cell Dev. Biol., vol. 11, pp. 35-71, 1995.			
MA		J. Eller, et al., "Modelling Thrombopoiesis Regulation-I; Model Description and Simulation Results," Comput. Math. Applic., vol. 14, no. 9-12, pp. 841-848, 1987.			
MA		G. K. von Schulthess, et al., "Oscillating platelet counts in healthy individuals: Experimental investigation and quantitative evaluation of thrombocytopoietic feedback control," Scand J Haematol, vol. 36, pp. 473-479, March 8, 1986.			
MA		L. A. Harker, et al., "Dose-Response Effects of Pegylated Human Megakaryocyte Growth and Development Factor on Platelet Production and Function in Nonhuman Primates," The American Society of Hematology, Blood, vol. 88, no. 2, pp. 511-521, July 15, 1996.			

Examiner Signature	MA Moran	Date Considered	1/14/04
--------------------	----------	-----------------	---------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kind Codes of USPTO Patent Documents at www.uspto.gov, MPEP 901.04 or in the comment box of this document. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to indicate here if English language Translation is attached.

RECEIVED  
TECH CENTER 1600  
JUL 13 2003

Substitute for Form 1449 A & B/PTO				Application Number	09/827,229
				Confirmation Number	7712
				Filing Date	April 06, 2001
				First Named Inventor	Zvia AGUR
				Art Unit	1631
				Examiner Name	Marjorie A. MORAN
Sheet	2	of	4	Attorney Docket Number	Q63893

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		Number	Kind Code <sup>2</sup> (if known)		
	US				

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)		

OTHER ART - NON PATENT LITERATURE DOCUMENTS							
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city, and/or country where published.					Translation <sup>6</sup>
MSM		P. A. Fielder, "Regulation of Thrombopoietin Levels by c-mpl-Mediated Binding to Platelets," The American Society of Hematology, Blood, vol. 87, no. 6, pp. 2154-2161, March 15, 1996.					
MSM		John E. J. Rasko et al., "Molecules in focus; The thrombopoietic factor, Mpl-ligand," The International Journal of Biochemistry & Cell Biology, vol. 30, pp. 657-660, 1998.					
MSM		F. J. de Sauvage, et al., "Physiological Regulation of Early and Late Stages of Megakaryocytopoiesis by Thrombopoietin," Departments of Molecular Biology, Cell Genetics, vol. 183, pp. 651-656, February 1996.					
MSM		F. Tacke, et al., "Endogenous serum levels of thrombopoietic cytokines in healthy whole-blood and platelet donors: implications for plateletpheresis," British Journal of Haematology, vol. 105, pp. 511-513, 1999.					
MSM		S. A. Burstein, et al., "Megakaryopoiesis and platelet formation," Williams Hematology, 5 <sup>th</sup> ed., Ch. 118, McGraw-Hill, Inc., 1995.					
MSM		R. Schofield, et al., "Self-Maintenance Capacity of CFU-S," Journal of Cellular Physiology, vol. 103, pp. 355-362, 1980.					
MSM		M. Rosendaal, et al., "Organization of Haemopoietic Stem Cells: The Generation-Age Hypothesis," Cell Tissue Kinet., vol. 12, pp. 17-29, 1979.					
MSM		A. Iliadis, et al., "Optimizing Drug Regimens in Cancer Chemotherapy by an Efficacy-Toxicity Mathematical Model," Computers and Biomedical Research, vol. 33, pp. 211-226, 2000.					
MSM		F. L. Pereira, et al., "A new optimization based approach to experimental combination chemotherapy," Frontiers Med. Biol. Engng., vol. 6, no. 4, pp. 257-268, 1995.					
*Hassin Agur, "Optimizing Chemotherapy Scheduling Using Search Heuristics," pp. 2-36							
MSM		Kenji Terashi, et al., "Close Association between Clearance of Recombinant Human Granulocyte Colony-Stimulating Factor (G-CSF) and G-CSF Receptor on Neutrophils in Cancer Patients," Antimicrobial Agents and Chemotherapy, vol. 43, no. 1, pp. 21-24, January 1999.					
MSM		T. H. Price, et al., "Effect of Recombinant Granulocyte Colony-Stimulating Factor on Neutrophil Kinetics in Normal Young and Elderly Humans," The American Society of Hematology, vol. 88, no. 1, pp. 335-340, July 1, 1996.					
MSM		B. I. Lord, et al., "The kinetics of human granulopoiesis following treatment with granulocyte colony-stimulating factor in vivo," Proc. Natl. Acad. Sci. USA, vol. 86, pp. 9499-9503, December 1989.					

Examiner Signature	MSM	Date Considered	11/14/04
--------------------	-----	-----------------	----------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov), MPEP 901.04 or in the comment box of this document. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to indicate here if English language Translation is attached.

<p>Substitute for Form 1449 A &amp; B/PTO</p> <p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b></p> <p><i>(use as many sheets as necessary)</i></p>				<p><i>Complete if Known</i></p>															
<i>JUL 08 2003</i> <i>RECEIVED</i> <i>SEARCHED</i> <i>INDEXED</i> <i>FILED</i> <i>APR 6 2001</i> <i>Q63893</i>				<table border="1"> <tr> <td>Application Number</td> <td>09/827,229</td> </tr> <tr> <td>Confirmation Number</td> <td>7712</td> </tr> <tr> <td>Filing Date</td> <td>April 6, 2001</td> </tr> <tr> <td>First Named Inventor</td> <td>Zvia AGUR</td> </tr> <tr> <td>Art Unit</td> <td>1631</td> </tr> <tr> <td>Examiner Name</td> <td>Marjorie A. MORAN</td> </tr> <tr> <td>Attorney Docket Number</td> <td>Q63893</td> </tr> </table>		Application Number	09/827,229	Confirmation Number	7712	Filing Date	April 6, 2001	First Named Inventor	Zvia AGUR	Art Unit	1631	Examiner Name	Marjorie A. MORAN	Attorney Docket Number	Q63893
Application Number	09/827,229																		
Confirmation Number	7712																		
Filing Date	April 6, 2001																		
First Named Inventor	Zvia AGUR																		
Art Unit	1631																		
Examiner Name	Marjorie A. MORAN																		
Attorney Docket Number	Q63893																		
Sheet	3	of	4																

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		Number	Kind Code <sup>2</sup> (if known)		
		US			

FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Translation <sup>6</sup>
		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			

OTHER ART - NON PATENT LITERATURE DOCUMENTS			Translation <sup>6</sup>
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city, and/or country where published.	
MSW		J. Y. Mary, "Normal Human Granulopoiesis Revisited. 1. Blood Data," <i>Biomedicine &amp; Pharmacotherapy</i> , vol. 38, pp. 33-43, 1984.	
MSW		J. Y. Mary, "Normal Human Granulopoiesis Revisited. II. Bone Marrow Data," <i>Biomedicine &amp; Pharmacotherapy</i> , vol. 38, pp. 66-77, 1984.	
MSW		C. Dresch, et al., "Growth fraction of myelocytes in normal human granulopoiesis," <i>Cell Tissue Kinet.</i> vol. 19, pp. 11-22, 1986.	
MSW		S. Schmitz, et al., "The effect of continuous G-CSF application in human cyclic neutropenia: a model analysis," <i>British Journal of Haematology</i> , vol. 90, pp. 41-47, 1995.	
MSW		S. Schmitz, et al., "Quantification of the cell kinetic effects of G-CSF using a model of human granulopoiesis," <i>International Society for Experimental Hematology, Experimental Hematology</i> , vol. 21, pp. 755-760, 1993.	
MSW		L. A. Harker, et al., "Regulation of Platelet Production and Function by Megakaryocyte Growth and Development Factor in Nonhuman Primates," <i>The American Society of Hematology</i> , no. 5, pp. 1833-1844, March 1996.	
MSW		Warren S. Alexander, "Thrombopoietin," <i>The Walter and Eliza Hall Inst. for Medical Research, Growth Factors</i> , vol. 17, pp. 13-24, 1999.	
MSW		Kenneth Kaushansky, "Thrombopoietin: The Primary Regulator of Platelet Production," <i>The Journal of The American Society of Hematology, Blood</i> , vol. 86, no. 2, pp. 419-431, July 15, 1995.	
MSW		Saroj Vadhan-Raj, "Recombinant Human Thrombopoietin: Clinical Experience and In Vivo Biology," <i>Seminars in Hematology</i> , vol. 35, No. 3, pp. 261-268, July 1998.	
MSW		Laurence A. Harker, "Physiology and clinical applications of platelet growth factors," <i>Curr Opin Hematol</i> , vol. 6, pp. 127-134, 1999.	
MSW		Jack Levin, "Thrombopoietin -- Clinically Realized?" <i>The New England Journal of Medicine</i> , vol. 336, no. 6, pp. 1-3, February 6, 1997.	
MSW		G. Somlo, et al., "Recombinant Human Thrombopoietin in Combination with Granulocyte Colony-Stimulating Factor . . . High-Dose Chemotherapy," <i>The American Society of Hematology, Blood</i> , vol. 93, no. 9, pp. 2798-2806, May 1, 1999.	
MSW		K. J. Neelis, et al., "The Efficacy of Single-Dose Administration of Thrombopoietin with Coadministration . . . Myelosuppressed Rhesus Monkeys," <i>The American Society of Hematology, Blood</i> , vol. 90, no. 7, pp. 2565-2573, October 1, 1997.	

Examiner Signature	M. A. Myrman	Date Considered	1/14/04
--------------------	--------------	-----------------	---------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov), MPEP 901.04 or in the comment box of this document. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to indicate here if English language Translation is attached.

Substitute for Form 1449 A & B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	09/827,229
(use as many sheets as necessary)				Confirmation Number	7712
				Filing Date	April 06, 2001
				First Named Inventor	Zvia AGUR
				Art Unit	1631
				Examiner Name	Marjorie A. MORAN
Sheet 4		of 4	Attorney Docket Number Q63893		

RECEIVED  
U.S. PATENT AND TRADEMARK OFFICE  
JULY 8 2003  
1003  
1003  
1003

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		Number	Kind Code <sup>2</sup> (if known)		
	US				

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Translation <sup>6</sup>
		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)		

OTHER ART - NON PATENT LITERATURE DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city, and/or country where published.			Translation <sup>6</sup>
MM		L. J. Murray, et al., "Thrombopoietin Mobilizes Cd34+ Cell Subsets Into Peripheral Blood And Expands Multilineage Progenitors In Bone Marrow Of Cancer Patients With Normal Hematopoiesis," Experimental Hematology, vol. 26, pp. 207-216, 1998.			
MM		R. L. Basser, et al., "Randomized, Blinded, Placebo-Controlled Phase I Trial of Pegylated Recombinant Human Megakaryocyte Growth and Development Factor with Filgrastim after Dose-Intensive Chemotherapy in Patients with Advanced Cancer," The American Society of Hematology, Blood, Vol. 89, no. 9, pp. 3118-3128, 1997.			
MM		D. Zucker-Franklin, "The Ultrastructure of Megakaryocytes and Platelets," Dept. of Medicine and Rheumatic Diseases Study Group, New York, The Platelets, Ch. 55, pp. 1553-1629.			
MM		L. A. Harker, et al., "Thrombokinetics in Man," The Journal of Clinical Investigation, vol. 48, pp. 963-974, 1969.			
MM		Laurence H. Harker, "Thrombokinetics in Idiopathic Thrombocytopenic Purpura," British Journal of Haematology, pp. 95-104, 1970.			
MM		R. Sungaran, et al., "Localization and Regulation of Thrombopoietin mRNA Expression in Human Kidney, Liver, Bone Marrow, and Spleen Using In Situ Hybridization," The American Society of Hematology, Blood, vol. 89, no. 1, pp. 101-107, 1997.			
MM		Y. Nagata, et al., "Serum Thrombopoietin Level is not Regulated by Transcription but by the Total Counts of both Megakaryocytes and Platelets during Thrombocytopenia and Thrombocytosis," Tsukuba Life Science Center, Thrombosis and Haemostasis, vol. 77, pp. 808-814, 1997.			
MM		H. Nagahisa, et al., "Bone Marrow Stromal Cells Produce Thrombopoietin and Stimulate Megakaryocyte Growth and Maturation but Suppress Proplatelet Formation," The American Society of Hematology, Blood, vol. 87, no. 4, pp. 1309-1316, February 15, 1996.			
MM		I. Athanassios, et al., "Comparison Between Optimata's Claims and Contemporary, 'state of the art' in Optimizing of Anticancer Chemotherapy," Computers and Biomedical Research, vol. 33, pp. 211-226, 2000.			
MM		Hui-Chi Hsu, et al., "Circulating Levels of Thrombopoietic and Inflammatory Cytokines in Patients with Clonal and Reactive Thrombocytosis," J Lab Clin Med, vol. 134, no. 4, pp. 392-397, 1999.			

Examiner Signature	Marjorie A. MORAN	Date Considered	11/14/04
--------------------	-------------------	-----------------	----------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov), MPEP 901.04 or in the comment box of this document. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to indicate here if English language Translation is attached.